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Unexplained Immunodeficiency and Opportunistic Infections in Infants -- New York, New Jersey, California

CDC has received reports of four infants (under 2 years of age) with unexplained cellular immunodeficiency and opportunistic infections.

Case 1: The infant, a black/hispanic male weighing 5 lb 14 oz, was born in December 1980 following a 36-38-week pregnancy. Pregnancy had been complicated by bleeding in the fourth month and by preeclampsia in the ninth month. The infant was well until 3 months of age, when oral candidiasis was noted. At 4 months, hepatosplenomegaly was observed, and at 7 months, he had staphylococcal impetigo. Growth, which had been slow, stopped at 9 months. Head circumference, which had been below the third percentile, also stopped increasing. At 9 months, serum levels of IgG and IgA were normal; IgM was high-normal. T-cell studies were normal, except for impaired in-vitro responses to Candida antigen and alloantigen.

At 17 months of age, the infant had progressive pulmonary infiltrates, as well as continuing oral candidiasis, and was hospitalized. Mycobacterium avium-intracellulare was cultured from sputum and bone marrow samples. A CAT scan of the head revealed bilateral calcifications of the basal ganglia and subcortical regions of the frontal lobes. Repeat immunologic studies done at age 20 months showed lymphopenia, decreased numbers of T-lymphocytes, and severely impaired T-cell function in vitro; immunoglobulin determinations are pending. The infant remains alive and is receiving therapy for his mycobacterial infection.

The infant's mother, a 29-year-old resident of New York City, gave a history of intravenous drug abuse. Although she was in apparently good health at the time of the infant's birth, she developed fever, dyspnea, and oral candidiasis in October 1981. One month later, she was hospitalized and died of biopsy-proven Pneumocystis carinii pneumonia (PCP). She had been lymphopenic during the hospitalization; further immunologic studies were not done. At autopsy, no underlying cause for immune deficiency was found.

Case 2: The infant, a Haitian male weighing 6 lb 11 oz, was born in January 1981 following full-term pregnancy. The immediate postpartum period was complicated by respiratory distress. Diarrhea developed at 2 weeks of age and persisted. His physical development was retarded. At 5 months, he was hospitalized because of fever and diarrhea. On examination, he had hepatosplenomegaly, lymphadenopathy, and otitis media. While on antibiotics, he developed pulmonary infiltrates. An open lung biopsy revealed Pneumocystis carinii, Cryptococcus neoformans, and cytomegalovirus. Serum IgG, IgA, and IgM concentrations were elevated. The percentage of T-lymphocytes was decreased, but T-cell response to mitogens was normal. The infant died of respiratory insufficiency at 7H months of age. At autopsy, the thymus, spleen, and lymph nodes showed lymphocyte depletion.

His parents were residents of Brooklyn, New York; their health status is unknown.

Case 3: The infant, a Haitian male weighing 8 lb, was born in November 1981 following a normal, full-term pregnancy. He was apparently healthy until 5 months of age, when he was hospitalized with fever and respiratory distress. On examination, he had hepatosplenomegaly. A chest x-ray showed bilateral pulmonary infiltrates. Despite antibiotic therapy, the infant's condition deteriorated, and an open lung biopsy revealed PCP. Immunologic studies showed elevated serum concentrations of IgG, IgA and IgM, decreased percentage of T-lymphocytes, and impaired T-cell function in vitro. The infant died in May 1982. At autopsy, no cardiovascular anomalies were seen; the thymus was hypoplastic, but all lobes were present. His parents were residents of Newark, New Jersey; their health status is unknown.

Case 4: The infant, a white female weighing 5 lb, was born in April 1982 following a normal 35-week pregnancy. She was well until 2 months of age, when oral and vaginal Candida infections were noted. She responded to antifungal therapy, but at 5 months, candidiasis recurred, and she had hepatosplenomegaly. Immunologic evaluation showed that serum IgG, IgA, and IgM levels, normal at 2 months, were now elevated. The percentage of T-lymphocytes was decreased, and lymphocyte response to alloantigen was impaired. At 6 months of age, the infant was hospitalized because of fever and cough. Open lung biopsy revealed PCP. Despite appropriate antibiotic therapy, she died in November 1982.

The infant's mother, a 29-year-old resident of San Francisco, is a prostitute and intravenous drug abuser with a history of oral candidiasis and mild lymphopenia. She has had two other female children by different fathers. These half-sisters also have unexplained cellular immunodeficiency; one died of PCP. The children had not lived together.

None of the four infants described in the case reports was known to have received blood or blood products before onset of illness.

Other cases with opportunistic infections: Six additional young children with opportunistic infections (five with PCP, one with M. avium-intracellulare) and unusual cellular immunodeficiencies are under investigation. Three are male. All six children have died. One was a half-sister of the infant in Case 4.

Other cases without opportunistic infections: Physicians from New York City, New Jersey, and California have reported another 12 young children with immunodeficiencies similar to those seen in cases 1-4 but without life-threatening opportunistic infections. One is the other half-sister of the infant in Case 4. All the children are living; their ages range from 1 to 4 years. Eight are male. Clinical features seen in these 12 infants include: failure to thrive (83%), oral candidiasis (50%), hepatosplenomegaly (92%), generalized lymphadenopathy (92%), and chronic pneumonitis without a demonstrable infection (83%). Of the nine mothers for whom information is available, seven are reported to be intravenous drug abusers. None is Haitian. Reported by R O'Reilly, MD, D Kirkpatrick, MD, Memorial Sloan-Kettering Cancer Center, C Butkus Small, MD, R Klein, MD, H Keltz, MD, G Friedland, MD, Montefiore Hospital and Medical Center, K Bromberg, MD, S Fikrig, MD, H Mendez, MD, State University of New York, Downstate Medical Center, A Rubinstein, MD, Albert Einstein College of Medicine, M Hollander, MD, Misericordia Hospital Medical Center, F Siegal, MD, Mt Sinai School of Medicine, J Greenspan, MD, Northshore University Hospital, M Lange, MD, St Lukes-Roosevelt Hospital Center, S Friedman, MD, New York City Dept of Health, R Rothenberg, MD, State Epidemiologist, New York State Dept of Health; J Oleske, MD, C Thomas MD, R Cooper, MD, A de la Cruz, MD, St Michaels Medical Center, A Minefore, MD, St Josephs

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Editorial Note

Editorial Note: The nature of the immune dysfunction described in the four case reports is unclear. The infants lacked the congenital anomalies associated with Di George's syndrome. The immunologic features of high-normal or elevated immunoglobulin levels and T-lymphocyte depletion are not typical of any of the well-defined congenital immunodeficiency syndromes. They have, however, been described in a few children with variants of Nezelof's syndrome, a rare, poorly characterized illness of unknown etiology (1,2). The occurrence of immune deficiency in the infant in case 4 and in her half-sisters raises the possibility of an inherited disorder. However, inheritance would have to have occurred in a dominant manner, an inheritance pattern not previously described for immunodeficiency resembling that seen in these half-sisters.

It is possible that these infants had the acquired immune deficiency syndrome (AIDS). Although the mother of the infant in case 1 was not studied immunologically, her death from PCP was probably secondary to AIDS. The mothers of the other three infants were Haitian or intravenous drug abusers, groups at increased risk for AIDS (3). The immunologic features described in the case reports resemble those seen both in adults with AIDS (4) and in a child reported to have developed immunodeficiency following receipt of blood products from a patient with AIDS (5). Case 2 had essentially normal T-cell responses to mitogens in vitro. This finding is atypical for AIDS, but it has been seen in a few adult AIDS cases (6).

Although the etiology of AIDS remains unknown, a series of epidemiologic observations suggests it is caused by an infectious agent (3,5,7-9). If the infants described in the four case reports had AIDS, exposure to the putative "AIDS agent" must have occurred very early. Cases 2-4 were less than 6 months old when they had serious opportunistic infections. Case 1 had oral candidiasis beginning at 3 months of age, although M. avium-intracellulare infection was not documented until 17 months. Transmission of an "AIDS agent" from mother to child, either in utero or shortly after birth, could account for the early onset of immunodeficiency in these infants.

The relationship between the illnesses seen in the reported cases with severe opportunistic infection and the 12 infants without such infections is unclear at present. The immune dysfuction seen in the children and the sociodemographic profiles of the mothers appear similar in both groups. Prospective study of the 12 children is necessary to define the natural history of their illnesses and the possible relationship of their illnesses to AIDS.

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